REMARKS

Upon issuance of the Office Action dated October 27, 2009, claims 1, 4, 7-9, 14-26, 33-45 and 48-56 were pending in the application, and claims 8 and 49-56 were withdrawn from consideration as being drawn to a non-elected invention. In the present amendment, claims Claim 4, 10-13, 16 and 45-56 have been canceled; claims 1, 14, 15, 17-20, 24-26 and 35-37 have been amended; and new claim 57 has been added. Support for the amendments to the claims may be found throughout the specification and claims as originally filed. *No new matter has been added.*

Accordingly, upon entry of the amendments presented herein, claims 1, 14, 15, 17-26, 34-44 and 57 will be pending in the application. Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Acknowledgement of the Withdrawal of Previous Rejections

Applicants gratefully acknowledge the withdrawal of the previous rejections of claim 33 under 35 U.S.C. §112, second paragraph; claims 4, 9, 14-26, 33-45 and 48 under 35 U.S.C. §112, first paragraph; claims 14, 24, 33, 24, 36, 38, 38 and 39 under 35 U.S.C. §102(b) over Pasricha; claims 14 and 24 under 35 U.S.C. §102(b) over Dunant et al.; claims 45 and 48 under 35 U.S.C. §102(b) over Richardson et al.; and claims 45 and 48 under 35 U.S.C. §102(b) over Gusovsky et al.

Claim Objections

Applicants respectfully submit that the objection to claim 45 have been rendered moot by the cancellation of the claim.

Claim Rejections Under 35 U.S.C. §112

Applicants respectfully submit that the rejections of claim 4 as being indefinite, and of claims 45 and 48 for failing to comply with the enablement requirement have been rendered moot by the cancellation of these claims.

Claim Rejections Under 35 U.S.C. §102(b)

The rejection of claim 14-22, 24-26, 33-36, 38 and 39, 40 and 41-44 as being anticipated by Ruvkun et al. (US 2001/0029617) was maintained on the ground that "[i]t is intrinsic to the teachings of Ruvkun et al. that disruption of insulin signaling, which is caused by muscarinic antagonists, would extend adult lifespan of *C. elegans,*" (Office Action at p. 11).

Applicants respectfully disagree. However, solely in the interest of expediting prosecution of the application, the claims have been amended to specify that "the indicator of the cholinergic pathway is selected from the group consisting of EGL-8, RIC-8 and RIC-4, or a mammalian orthologue thereof." Accordingly, reconsideration and withdrawal of this rejection is requested.

Claim Rejections Under 35 U.S.C. §103

The rejection of claims 1, 4, 7 and 9 as being unpatentable over Ruvkun et al. in view of Gems & Riddle was maintained on the ground that, allegedly,

> After reading Ruvkun et al., and upon reading Gems and Riddle, the person of ordinary skill in the art would recognize that disruptions of gene expression in [*sic*] both the cholinergic and insulin signaling pathways leads to greater longevity. (Office Action at p. 16)

Claims 4, 7 and 9 have been canceled without prejudice. As amended, independent claim 1 is directed to a method of identifying an agent capable of extending the mature life phase of an organism by contacting an organisms having altered expression or activity of a *cholinergic pathway molecule selected from the group consisting of EGL-8, RIC-8 and RIC-4*, and altered expression of DAF-2 with a test agent, wherein the altered activity or expression of the cholinergic pathway molecule or the altered activity or expression of DAF-2 extends the mature life phase of the organism, assaying for the ability of the test agent to increase the lifespan of the organism, and selecting an agent that increases lifespan.

The presently claimed method is based on the unexpected finding that organisms containing combined mutations in EGL-8 and DAF-2, RIC-8 and DAF-2, or RIC-4 and DAF-2 showed an increase in life span that was longer than that observed in organisms containing either mutation alone (See specification, page 52, lines 1-9; page 53, lines 7-21; and page 56, lines 6-

24). These results indicated that the role of EGL-8, RIC-8 and RIC-4 in life span extension *is independent of DAF-2*.

In contrast, Ruvkun et al. teach that the muscarinic and insulin signaling pathways are linked and that "the cholinergic input to dauer recovery *depends on insulin-like signaling [DAF-21*," (paragraph [411], emphasis added). Gems and Riddle teach that mutations in the cholinergic/serotonergic pathway molecule, UNC-13, demonstrate a male specific increase in longevity. However, the combined teachings of these references fail to even suggest that molecules in the cholinergic pathway can act on independently of DAF-2 on life span extension. Indeed, mutations in DAF-2 (as taught by Ruvkun et al.) and mutations in UNC-13 (as taught by Gems and Riddle), when combined in the same organism result in the same life extension as observed in organisms containing mutations in DAF-2 alone, indicating that the role of UNC-13 in life span extension is dependent upon DAF-2 (see specification, page 49, lines 9-20). Neither reference alone or in combination teach or suggest that EGL-8, RIC-8 or RIC-4 play a role in lifespan extension, let alone that organisms containing a mutations in one of these molecules in combination with a mutation in DAF-2 demonstrate an increased lifespan that is greater than that observed in organisms containing a mutation in DAF-2 alone. It was both unexpected and surprising that the cholinergic pathway molecules EGL-8, RIC-8 and RIC-4 effect lifespan extension *independently of insulin-like signaling.*

Accordingly, at least in view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

The rejections of claim 20, 23 and 37 as being unpatentable over Ruvkun et al., were also maintained essentially for the reasons of record as set forth in the Office Action dated February 11, 2009. Specifically, Claim 23 was rejected as being unpatentable over Ruvkun et al. on the ground that although this reference does not explicitly disclose carrying out the longevity screening assays in the parasitic nematode *A. canimum,* it does disclose that the biochemical pathways found in *C. elegans* are also present in the nematode *A. caninum.* Claims 20 and 37 were also rejected as being unpatentable over Ruvkun et al. on the ground that it would have been obvious to substitute monitoring cellular localization in the assays for monitoring the effect of muscarinic agonists and antagonists on dauer formation disclosed by Ruvkun et al.

Applicants respectfully traverse these rejections. Claim 20, 23 and 37, and the claims from which they depend, are directed to a methods of identifying an agent capable of extending the mature life phase of an organism which include the steps of contacting an organism or cell having a cholinergic pathway with a test agent and assaying for the ability of the test agent to inhibit expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization altered expression or activity of an indicator of the cholinergic pathway selected from the group consisting of EGL-8, RIC-8 and RIC-4, or a mammalian orthologue thereof, and selecting and agent that inhibits the cholinergic pathway.

In contrast, the screening assays taught by Ruvkun et al. are focused on identifying agents that act molecules of the insulin signaling and TGFβ signaling pathways. Ruvkun et al. neither teach nor suggest identifying agents which increase lifespan by screening for agents that inhibit EGL-8, RIC-8 and RIC-4.

Accordingly, reconsideration and withdrawal of these rejections is respectfully requested.

CONCLUSION

In view of the above remarks, applicant believes the pending application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

A Petition for Extension of Time within which to respond and the requisite fees are submitted herewith. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 12-0080, under Order No. UMY-035RCE.

Dated: April 27, 2010

Respectfully submitted,

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